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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/557,423	04/21/00	BELOTSERKOVSKII B	A-68112-1/RF

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EXAMINER	
LOEB, B	
ART UNIT	**PAPER NUMBER**
1636	6

DATE MAILED: 01/17/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/557,423	BELOTSERKOVSKII ET AL.	
	Examiner	Art Unit	
	Bronwen M. Loeb	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *Nov. 29, 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-66, 108 and 112* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-66, 108 and 112* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

DETAILED ACTION

This action is in response to the restriction election dated November 29, 2000. Claims 66-107 and 109-111 have been cancelled. Claims 1-66, 108 and 112 are pending.

Election/Restrictions

1. Applicant's election without traverse of Group I in Paper No. 5 is acknowledged. Nonelected claims 67-107 and 109-111 have been cancelled. The restriction requirement is therefore moot.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because sequences were set forth however no CRF was filed, no paper sequence was filed and no attorney statement was filed. These sequences include: **Figures 9 and 16, pages 5-7, 11, 12, 38 and on p.45 line 20 is a sequence lacking a sequence identifier numbe**r. If the Sequence Listing required for the instant application is identical to that of another application, a letter may be submitted requesting transfer of the previously filed sequence information to the instant application. For a sample letter requesting transfer of sequence information, refer to MPEP 2422.05. Additionally, it is often convenient to identify sequences in figures by amending the Brief Description of the Drawings section (see MPEP 2422.02).

Applicants are required to comply with all of the requirements of 37 CFR 1.821 through 1.825. Any response to this office action that fails to meet all of these requirements will be considered non-responsive. The nature of the noncompliance with the requirements of 37 C.F.R. 1.821 through 1.825 did not preclude the continued examination of the application on the merits, the results of which are communicated below.

Specification

2. The disclosure is objected to because of the following informalities: Figure 2 lacks a clear indication of the claimed homology clamp and anchoring sequence. The significance of the filled-in squares versus the blank squares is not described in the specification.

Appropriate correction is required.

Claim Objections

3. Claim 43 is objected to because of the following informalities: In claim 43, lines 2-3, the phrase "a single stranded targeting polynucleotides" is improper grammar; "polynucleotides" should not be plural. Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 10, 14, 18-21, 31, 33-42, 52, and 54-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 10, the phrase "wherein at one of said targeting polynucleotides comprises protein nucleic acid" is vague and indefinite.

Claim 14 recites the limitation "said RecA protein species" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 18 recites the limitation "said single stranded nucleic acids" in line 1. There is insufficient antecedent basis for this limitation in the claim.

In claims 21, 42 and 63, the phrase "purification moieties" is vague and indefinite. While the specification provides a definition for "purification tag moieties" (p. 30, lines 25-28), it does not provide one for "purification moieties". It would be remedial to amend the claim language to read "purification tag moieties".

In claim 31 and 52, the phrase "wherein at least one of said targeting polynucleotides comprises protein-nucleic acid" is vague and indefinite. It is not clear what is meant by "polynucleotides comprises protein-nucleic acid" and the specification does not explicitly define this phrase. Is the protein bound non-covalently to the nucleic acid? Is the protein covalently conjugated to the nucleic acid?

Claim 33 recites the limitation "said recombinase" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 35 recites the limitation "said RecA protein species" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 36 recites the limitation "said recombinase" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 39 recites the limitation "said single stranded nucleic acids" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 54 recites the limitation "said recombinase" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 57 recites the limitation "said recombinase" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 60 recites the limitation "said single stranded nucleic acids" in line 1. There is insufficient antecedent basis for this limitation in the claim.

In claim 64, the term "containing" is vague and unclear because it is not legally defined as open or closed transitional language and thus renders the claim unclear.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

7. Claim 10, 31 and 52 have been examined assuming that the unclear phrases mean at least one of the targeting polynucleotides comprise a protein moiety attached to said polynucleotide. Claims 21, 42 and 63 have been examined assuming "purification moieties" refer to purification tag moieties.

8. Claims 1, 6, 8, 9-21, 22, 27, 29-42, 43, 48, 50-66 and 108 are rejected under 35 U.S.C. 102(e) as being anticipated by Pati et al (USP 5,948,653). Pati et al teach a composition comprising at least one recombinase and two substantially complementary

single stranded targeting polynucleotides, each containing a) at least one homology clamp that substantially corresponds to or is substantially complementary to a preselected target nucleic acid sequences and b) at least one anchoring sequence. Pati et al teach a composition comprising a double D-loop comprising a target nucleic acid and two substantially complementary single stranded targeting polynucleotides, each containing a) at least one homology clamp and b) at least one anchoring sequence. Pati et al teach a composition comprising a double D-loop comprising a target nucleic acid and a single stranded targeting polynucleotide comprising a first homology clamp, a second homology clamp and at least one anchoring sequence. See col. 19, line 61-col. 20, line 3, col. 22, lines 31-59, Figures 10, 13B, and 13C, and ex.5, col. 53-58, wherein the "anchoring sequence" in the instant specification reads on the "internal homology clamp" of Pati et al and wherein Figure 13B, for instance, illustrates a single stranded targeting polynucleotide comprising a first and second homology clamp and at least one anchoring sequence. The composition wherein the nucleic acids may be DNA, RNA or a hybrid of both is taught in col. 16, lines 19-30. The composition wherein the recombinase is a prokaryotic recombinase is taught in col. 23, line 35- col. 24, line 8 and wherein the recombinase is prokaryotic RecA protein and wherein the RecA is from E. coli is taught in col. 24, lines 8-15. The composition wherein the recombinase is an eukaryotic recombinase is taught in col. 24, lines 15-20 and wherein it is Rad51 is taught in col. 24, lines 19 and 30. The composition wherein the eukaryotic recombinase is a complex of recombinase proteins is taught in col. 24, lines 22-23. The composition where at least one single stranded nucleic acid contains at least one

substituent is taught in col. 7, lines 17-29 and col. 27, lines 40-42. The composition wherein the substituent is a chemical substituent is taught in col. 27, line 40- col. 28, line 5 and wherein the substituent is a protein is taught in col. 27, lines 58-59 and 65. The composition wherein the substituent is selected from the group consisting of intercalators, cross-linking moieties, labels, photoactive moieties, nucleic acid scission inducing moieties, purification moieties and nucleic acid modification moieties is taught in col. 27, lines 40-col. 28, lines 24. A cell containing the composition is taught in col. 28, lines 65-67, wherein the cell is eukaryotic is taught in col. 29, lines 63-65 and wherein it is prokaryotic is taught in col. 29, line 28. A kit comprising at least one recombinase and two substantially complementary single stranded targeting polynucleotides, each containing at least one homology clamp and at least one anchoring sequence is taught in col. 35, lines 58-59.

9. Claims 1, 6, 7, 12-14, 18-22, 27, 30, 33-35, 39-42 rejected under 35 U.S.C. 102(b) as being anticipated by Sena et al (USP 5,273,881). Sena et al teach a composition comprising at least one recombinase and two substantially complementary single stranded targeting polynucleotides, each containing a) at least one homology clamp that substantially corresponds to or is substantially complementary to a preselected target nucleic acid sequences and b) at least one anchoring sequence. Sena et al teach a composition comprising a double D-loop comprising a target nucleic acid and two substantially complementary single stranded targeting polynucleotides, each containing a) at least one homology clamp and b) at least one anchoring sequence. See Figure 9G, col. 3, lines 44-53, and col. 4, lines 1-8 wherein the

"anchoring sequence" of the instant invention reads on the complementary end terminal extensions taught by Sena et al. The composition wherein the recombinase is a prokaryotic recombinase is taught in col. 7, lines 27-46 and wherein the recombinase is prokaryotic RecA protein and wherein the RecA is from E. coli is taught in col. 7, lines 36-49. The composition where at least one single stranded nucleic acid contains at least one substituent is taught in col. 4, lines 16-21 and col. 5, lines 53-55. The composition wherein the substituent is a chemical substituent is taught in col. 5, lines 57-60 and wherein the substituent is a protein is taught in col. 5, lines 57-60. The composition wherein the substituent is selected from the group consisting of labels, photoactive moieties, nucleic acid scission inducing moieties, and purification moieties is taught in col. 4, lines 31-46 and col. 5, lines 53-60.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claim 112 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pati et al. Pati et al is applied as above. Pati et al does not explicitly disclose a composition wherein a protein is bound to the anchoring sequence. Pati et al teach the use of the composition to target chemical substituents to a predetermined DNA sequence using homologous pairing to produce sequence-specific localization of polynucleotides, for instance loading sites for transcription factors and/or RNA polymerase. See col. 7, lines 29-39. At the time the invention was made it would have been obvious to one of ordinary skill in the art to have the anchoring sequence encode a particular protein-binding site to which the protein would bind. One of ordinary skill in the art would be motivated to do this to increase the effective concentration of the protein in the vicinity of the targeted nucleic acid sequence, for instance, to increase the rate of homologous recombination or to enhance transcription repression with a repressor protein.

13. Claims 1-3, 6, 8, 9-21, 22-24, 27, 29-42, 43-45, 48, 50-66 and 108 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pati et al as applied to claims1, 6, 8, 9-21, 22, 27, 29-42, 43, 48, 50-66 and 108 above, and further in view of Helene et al (Biochimica et Biophysica Acta (1990) 1049:99-125). Pati et al is applied as above. Pati et al does not explicitly teach: a composition further comprising a secondary probe, wherein said probe is substantially complementary to at least one of said anchoring sequences; a composition wherein said anchoring sequences form a triplex anchor.

Helene et al teach providing a probe which forms a triplex structure as a means to regulate or stop transcription. See pp. 100-102 and Figures 1 and 3a. At the time the invention was made, it would have been obvious to one of ordinary skill in the art to use the probe of Helene et al in the composition of Pati et al, and to use the triplex anchor taught by Helene et al in the composition of Pati et al. One would have been motivated to do so since both references deal with methods of gene regulation using complementary DNA sequences. See Pati et al, col. 8, line 54-col. 9, line 2, and Helene et al, pp. 99-100 Introduction.

14. Claims 1, 5-8, 9-21, 22, 26-42, 43, 47-66 and 108 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pati et al as applied to claims 1, 6, 8, 9-21, 22, 27, 29-42, 43, 48, 50-66 and 108 above, and further in view of Barton (USP 5,225,556). Pati et al does not teach a composition wherein the anchoring sequences form a Z-DNA anchor; a composition wherein the anchoring sequences form an A-DNA anchor. Barton teaches a chemical probe specific for Z-DNA sequences and A-DNA sequences that may be used for labeling Z-DNA or A-DNA sequences. See Abstract, col. 4, lines 31-34, and col. 5, lines 26-30 and 34-37. At the time the invention was made, it would have been obvious to one of ordinary skill in the art to use anchor sequences that form Z-DNA or A-DNA. One of ordinary skill in the art would have been motivated to do so in order to use the specific chemical probe of Barton in order to label specifically the complexes formed by the composition with the target nucleic acid.

15. Claims 1, 4, 6, 8, 9-21, 22, 25, 27, 29-42, 43, 46, 48, 50-66 and 108 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pati et al as applied to claim claims

1, 6, 8, 9-21, 22, 27, 29-42, 43, 48, 50-66 and 108 above, and further in view of Simonsson et al (Nucleic Acids Research (1998) 26:1167-1172). Pati et al does not teach the composition wherein the anchoring sequences form a quadruplex anchor. At the time the invention was made, it would have been obvious to one of ordinary skill in the art to use a quadruplex anchor in the composition of Pati et al. One would have been motivated to do so because it was well known that quadruplex sequences are very stable (see Simonsson et al, p.1169-1170, Discussion) and forming a stable multistrand complex to inhibit transcription is taught by Pati et al (col. 8, line 63-col. 9, line 3).

Conclusion

Claims 1-66, 108 and 112 are rejected.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bronwen M. Loeb whose telephone number is (703) 605-1197. The examiner can normally be reached on Monday through Friday, from 8:30 AM to 5:00 PM. A phone message left at this number will be responded to as soon as possible (usually no later than the next business day after receipt by the examiner).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Richard Schwartz, can be reached on (703) 308-1133.

Any inquiry of a general nature or relating to the status of this application should be directed to Dianiece Jacobs, Patent Analyst whose telephone number is (703) 305-3388.

Bronwen M. Loeb, Ph.D.
Patent Examiner
Art Unit 1636

January 12, 2001

ROBERT A. SCHWARTZMAN
PRIMARY EXAMINER